

REMARKS

Claims 1 and 59 have been amended to more particularly point out the claimed subject matter. Support for such claim amendments can be found throughout the specification (e.g., page 32, lines 16-21; and Tables 6-7 on pages 98-103). Claims 5 and 14 have been amended solely to correct claim dependency. No new matter has been introduced and no new issue has been raised. The amendments have been made solely to expedite allowance. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants note with appreciation that the Examiner has withdrawn the previous rejections under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a) (citing Bennett et al., Khvorova et al., or Robbins et al.) as well as the rejection under 35 U.S.C. § 103(a) (citing Miyagishi et al., Promega, and Khvorova et al.). However, the Examiner has cited new art for claim rejections.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Claim Rejections under 35 USC § 112, Second Paragraph

The Examiner asserts that claims 5 and 14 are indefinite for depending from cancelled claim 3. In response, Applicants have amended claims 5 and 14 to correct claim dependency, rendering the rejection moot.

Claim Rejections under 35 USC § 102(b) or 35 USC § 103(a)

Claims 1, 7-11, 16, and 59 are rejected under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a) as being anticipated by or obvious over Monia et al. (Patent No. 6,270,030). Applicants traverse this rejection to the extent it is maintained over the claims as amended.

As an initial matter, Applicants note that page 3 of the Office Action characterizes this rejection as both § 102(e) and § 102(b). Applicants will address this rejection as if it is a 102(b) rejection. Clarification is respectfully requested.

Solely to expedite prosecution, Applicants have amended independent claims 1 and 59 to more particularly point out the technical features (structural and functional) of the nucleic acid compound. Support for the claim amendments can be found throughout the specification (e.g., page 32, lines 16-21; and Tables 6-7 on pages 98-103). For example, claim 1 as amended recites an isolated nucleic acid compound comprising a nucleotide sequence of between 20 and 35 nucleotides which is 100% complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell, wherein the nucleic acid compound is an antisense nucleic acid compound comprising one or more modified backbone or base moieties, and wherein the modified antisense nucleic acid comprises at least one 2'-O-alkylated ribonucleotide.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1978).

Applicants contend that Monia et al. fail to satisfy the criteria for anticipating the present invention. Monia et al. describe antisense compounds for modulating the expression of C/EBP beta (see, e.g., the abstract). However, Monia et al. do **not** teach or suggest compounds for decreasing expression of EphB4. More specifically, Monia et al. fail to teach or suggest an antisense nucleic acid compound comprising a nucleotide sequence of between 20 and 35 nucleotides which is 100% complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. The SEQ ID cited by the Examiner in the attached sequence alignment (namely SEQ ID NO: 41) has a two-bp mismatch with an EphB4 region, thereby lacking the technical features as recited in amended claim 1 or 59. Accordingly, Monia et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Monia et al.

Applicants further submit that Monia et al. do not render obvious the instant claims. According to the Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 In View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* (Federal Register Vol.

72, No. 195 at pages 57,526-57,535) (effective October 10, 2007) (“the Guidelines”), a § 103 claim rejection based on a purported teaching, suggestion or motivation to combine prior art references to arrive at the claimed invention must support a conclusion of obviousness by including: (1) a finding that there was some teaching, suggestion or motivation to modify or combine the cited references; (2) a finding that there was a reasonable expectation of success; and (3) whatever additional findings based on the *Graham* factual inquiries may be necessary in view of the specific facts. In particular, the Supreme Court stated *in KSR*:

“Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. **To facilitate review, this analysis should be made explicit.** See *In re Kahn*, 441 F. 3d 977, 988 (CA Fed. 2006) (‘[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness’)” (emphasis added).

In this case, the Examiner has not satisfied the requirement of establishing a prima facie case of obviousness against claims 1 and 59. The instant claims relate to nucleic acid compounds for decreasing expression of EphB4, whereas Monia et al. are concerned with modulation of expression of C/EBP beta, a molecule that is distinct from EphB4. Indeed, Monia et al. are absolutely silent on EphB4 as a target for antisense compounds, let alone antisense compounds that comprise a nucleotide sequence of between 20 and 35 nucleotides which is 100% complementary to a region of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases expression of EphB4 in a cell. In the absence of any suggestion in the cited art that EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to design EphB4-targeted nucleic acids as claimed in this application. In addition, there is no reasonable expectation of success for a skilled artisan to arriving at the claimed invention. Applicants further note that the Examiner has not provided articulated reasoning with some rational underpinning to support this legal conclusion of obviousness.

In view of the above, Monia et al. do not anticipate or render obvious the instant claims as amended. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance. Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. **VASG-P01-001** from which the undersigned is authorized to draw.

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Respectfully submitted,

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